PATENT
Customer Number: 22,852
Attorney Docket No. 07705.0001-01000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Brian ZAMBROWICZ et al.	)	Group Art Unit: 1632
	)	
Application No.: 10/797,613	)	Examiner: Shin Lin CHEN
	)	
Filed: March 9, 2004	)	Confirmation No.: 3971
	)	
For: VECTORS FOR GENE MUTAGENESIS AND GENE DISCOVERY	)	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION UNDER 37 C.F.R. § 1.132

We, Brian Zambrowicz, Glenn A. Friedrich, and Arthur T. Sands, do hereby make the following declaration:

1. We are three of four inventors named on U.S. Patent Application No. 10/797,613 ("the '613 application"). The other inventor named on the '613 application is Stan Lilleberg.

2. We are also three of four inventors named on U.S. Patent No. 6,207,371 ("the '371 patent"). The other inventor named on the '371 patent is Allan Bradley.

3. We understand that the Examiner has rejected claims 34 to 39 and 42 to 46 of the '613 application in view of certain material disclosed in the '371 patent. Specifically, we understand that the Examiner stated that:

> [The '371 patent] discloses VICTR3-5 gene trap vectors comprising a promoter, such as PGK promoter, a selectable marker, such as βgeo or HSV-Tk, and a splice donor sequence (e.g. column 7, lines 20-21, paragraph bridging columns 9-10, column 15, lines 41-54). The gene trap vector can be represented in retroviral form in retroviral vectors (e.g. column 7-8). Mouse ES cells are transfected with the gene trap vector to introduce mutation in the gene of the mouse genome and the ES cells can be injected into a blastocyst and become incorporated into normal development and ultimately the germ line so as to produce mutant transgenic m[ic]e (e.g. column[s] 15-16). [The '371 patent] further teaches identifying mutated gene sequence in the genome by RT-PCR [with] the mRNA isolated from the ES cells and using primers specific to the trapped, fusion transcript for PCR amplification and sequencing reaction to determine the sequence of the fusion transcript (e.g. section 5.2.2, column[s] 16-17).

Office Action mailed July 19, 2006, at pages 11 to 12.

4. A copy of claims 34 to 46, with intended amendments, is attached as Exhibit A. We are the sole inventors of the attached claims 34 to 39 and 42 to 46, with the intended amendments. We are also the sole inventors of the material in the '371 patent cited by the Examiner as set forth in paragraph 3 above.

5. Allan Bradley is not an inventor of the material in the '371 patent cited by the Examiner as set forth in paragraph 3 above.

6. Stan Lilleberg is not an inventor of currently rejected claims 34 to 39 and 42 to 46 of the '613 application.

7. We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: Jan. 16, 2007 By: _____
Brian Zambrowicz

Dated: _____ By: _____
Glenn A. Friedrich

Dated: Jan. 16, 2007 By: _____
Arthur T. Sands

EXHIBIT A

CLAIMS WITH INTENDED AMENDMENTS

34. (Currently amended) A method of making a transgenic mouse comprising a vector, comprising:

a) introducing a vector into a collection of ~~murine~~ mouse embryonic stem (ES) cells, wherein the vector comprises a 3′ gene trap cassette, comprising in operable combination:

i) a promoter;

ii) an exon sequence located 3′ from and expressed by said ~~first~~ promoter, said exon sequence not encoding an activity conferring antibiotic resistance; and

iii) a splice donor sequence located at the 3′ end of said exon sequence;

wherein the vector does not encode a sequence that mediates the polyadenylation of an mRNA transcript encoded by said exon sequence;

b) selecting ~~a murine ES cell~~ mouse ES cells that comprise[[s]] the vector integrated into the genome; ~~and~~

c) identifying at least one mouse ES cell comprising the vector, wherein the integration of said vector results in the mutation of a gene of the mouse, and wherein the mutated gene has been identified after integration of the vector; and

[[c)]] d) making a transgenic mouse comprising the vector from at least one identified ~~the selected murine~~ mouse ES cell that comprises the vector.

35. (Currently amended) The method of claim 34, wherein the vector from ~~the selected murine~~ at least one identified mouse ES cell that comprises the vector is non-homologously incorporated into the genome of at least one cell in the transgenic mouse.

36. (Canceled) ~~The method of claim 35, further comprising identifying at least one trapped cellular exon after (b).~~

37. (Canceled) ~~The method of claim 35, further comprising identifying at least one trapped cellular exon after (c).~~

38. (Previously presented) The method of claim 34, wherein the transgenic mouse comprising the vector is a somatic transgenic mouse.

39. (Previously presented) The method of claim 34, wherein the transgenic mouse comprising the vector is a germ line transgenic mouse.

40. (Currently amended) The method of claim 34, wherein the exon sequence additionally encodes an internal ribosome entry site operatively positioned between said ~~splice acceptor~~ promoter and an initiation codon of said exon sequence.

41. (Currently amended) The method of claim 34, wherein the vector additionally comprises in the region upstream of ~~between said polyadenylation sequence and~~ said promoter at least one of a transcription termination sequence, a 3′ terminal exon, and a sequence encoding a self-cleaving RNA.

42. (Previously presented) The method of claim 34, wherein the exon sequence encodes a marker selected from an enzymatic marker, a recombinase, and a fluorescent marker.

43. (Previously presented) The method of claim 42 wherein the marker is a fluorescent marker.

44. (Previously presented) The method of claim 34, wherein the vector is selected from a viral vector and a retroviral vector.

45. (Currently amended) The method of claim [[36]] 34, wherein the mutated gene has been identified by a method comprising: ~~identifying at least one trapped cellular exon comprises:~~

a) obtaining a chimeric transcript resulting from splicing of the exon sequence from the vector to a second exon sequence, wherein the second exon sequence is from the genome of the ES cell;

b) reverse transcribing said chimeric transcript to produce a cDNA template; and

c) determining the polynucleotide sequence of the cDNA template.

46. (Canceled) ~~The method of claim 37, wherein the identifying at least one trapped cellular exon comprises:~~

~~a) obtaining a chimeric transcript resulting from splicing of the exon sequence from the vector to a second exon sequence, wherein the second exon sequence is from the genome of the transgenic mouse;~~

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Dated: _____ By: _____
Brian Zambrowicz

Dated: 1/17/07 By: _____
Glenn A. Friedrich

Dated: _____ By: _____
Arthur T. Sands

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